DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta, GA 30333

February 14, 2014

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Charleston, West Virginia 25301

Dr. Tierney:

We are in receipt of the letter to Dr. Gupta from Dr. Flaherty concerning the use of body surface area for allometric dose translations in determining the "safe dose" for MCHM in drinking water. The use of body surface area (BSA) suggested by Dr. Flaherty has been used to predict blood levels for pharmaceuticals, but may not be appropriate for establishing screening comparison values for environmental exposures where little toxicological information is available.

The methodology ATSDR employed for establishing the MCHM screening value was similar to the approach it uses for establishing Minimal Risk Levels. ATSDR has published this method including the application of uncertainty factors in a number of places (Wheeler, 2002 [2];Chou, 1998[3]). Each new or revised ATSDR Toxicological Profile containing these Minimal Risk Levels undergoes rigorous peer review prior to being published. In addition, the ATSDR practice is similar to the procedures used by the US Environmental Protection Agency in developing their peer reviewed reference values (USEPA, 2011[3]).

We have evaluated the method suggested by Dr. Flaherty to estimate a human equivalent dose and have concerns with how his calculations were performed. First, we find that Dr. Flaherty began his extrapolation with a water concentration measured in parts per million (ppm); this is incorrect since he should have begun with an animal dose measured in mg/kg-day. Therefore, comparing any results to the 1 ppm screening level in water established by CDC is inappropriate. Secondly, it is inappropriate to estimate a human equivalent dose using constants for body surface area without modifying the uncertainty factor that is applied to the dose extrapolation from animals to humans.

We also want to emphasize that the 1 ppm screening level recommendation, and this response to Dr. Flaherty's letter have been reviewed and approved by an interagency workgroup composed of scientists from the National Institute of Environmental Health Sciences (NIEHS), National Toxicology Program (NTP), National Institutes of Health (NIH), Environmental Protection Agency (EPA) and Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry (CDC/ATSDR).

Please feel free to contact me if you have any additional questions or would like to discuss our response further.

1. Wheeler, J.S. and S. Chou, *Considerations and procedures in the derivation of ATSDR minimal risk levels.* Vaccine, 2002. 20 Suppl 3: p. S51-5.
2. Chou, C.H.S.J., J. Holler, and C.T. De Rosa, *Minimal risk levels (MRLs) for hazardous substances.* Journal of Clean Technology Environmental Toxicology and Occupational Medicine, 1998. 7(1): p. 1-24.
3. United States. Environmental Protection Agency. Risk Assessment Forum., *Recommended Use of Body Weight*3/4 *as the Default Method in Derivation of the Oral Reference Dose*. 2011, Washington, D.C.: Risk Assessment Forum, U.S. Environmental Protection Agency.

Sincerely,

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National Center for Environmental Health and
Agency for Toxic Substances and Disease Registry
Centers for Disease Control and Prevention